REMARKS

Applicants have amended claims 26, 32, 46, and 52-54, and added claims 55-57. As such, claims 26-32, 34-41, 46, and 52-57 are now pending in this application.

Claims 26, 46 and 54 are amended pursuant to the Examiner's suggestion made at the interview. The amendments replace "similar integral membrane protein" of influenza B anc C viruses with the specific names of those proteins – NB and CM2.[2] The amendments also make it clearer that the extracellular part of the M2, NB or CM2 membrane protein must be immunogenic to render the claimed product useful as an antigen and/or vaccine. Claim 54 is further amended to replace "presenting carrier" with "presenting peptide"; this amendment is consistent with the preceding part of the claim which states that the fusion product is encoded by a nucleic acid construct. Claim 32 is amended to clarify the meaning of T cell epitope by changing"of" to "recognized by." Claims 52 and 53 are amended to depend from claim 35, instead of claim 26, and to correct a typographical error. New claims 55-57 find support in claim 26 as originally filed.

These amendments are intended to promote clarity and to further define the scope of the invention. They do not introduce any new matter. In addition, none of the amendments raise new issues that would require further consideration or search. Applicants submit that these amendments would place the claims into condition for allowance, or at least present the rejected claims in better form for consideration on appeal, and should therefore be entered after the final rejection under 37 C.F.R.

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2 See also applicants' *Response to December 18, 2001 Office Action* filed April 18, 2002 ("previous Response"), which sets forth that a skilled person in the art would have known that the influenza B anc C counterparts of M2 are NB and CM2, respectively (pp. 8-9).

§ 1.116(a).

Applicants respectfully request reconsideration of the application in view of these claim amendments and the following discussion.

Rejections Under 35 U.S.C. § 112, 2nd ¶

Claims 26-32, 34-41, 46, 52 and 54 stand rejected for reciting the allegedly indefinite term "similar." During the interview, the Examiner suggested that the claim specifically recite NB and CM2, which are the respective influenza B and C counterparts of influenza A's M2. Applicants have amended independent claims 26, 46 and 54 accordingly. This amendment does not change the scope of the claims. It merely clarifies the meaning of "similar."

Claim 46 stands rejected for being in an improper product-by-process format. As discussed during the interview, the claim is in proper form. Applicants, thus, respectfully request the withdrawal of this rejection.

Claims 26, 46 and 54 stand rejected for reciting the allegedly indefinite term "an extracellular part." During the interview, Examiners Foley and Mosler suggested adding a functional term such as "immunogenic" to clarify the term. Applicants have amended the claims accordingly. This amendment is a clarification of the claims, not a narrowing of them. The claims were always directed to influenza "antigens." Those antigens must be immunogenic. That is the whole point.

Claim 54 is rejected for not providing an antecedent basis for "said animal species" in lines 4 and 5. Office Action, p. 4. As discussed during the interview, line 1 of the claim provides the necessary antecedent basis for the term. This rejection should therefore be withdrawn.

Rejections Under 35 U.S.C. § 112, 1st ¶

Claims 26-32, 34-41, 46, and 52-54 stand rejected for alleged lack of written description. Specifically, the Examiner contends that the specification lacks written description for "all or part of" SEQ ID No:1, 2, or 3. These claims also stand rejected for lack of written description for functional fragments of M2 or the immunoprotection of the possible fragments. Office Action, pp.5-6. During the interview, the Examiner suggested the amendments now made to the claims to overcome this rejection. Thus, applicants respectfully request the withdrawal of this rejection.

Claims 26-32, 34-41 and 52-54 stand rejected for lack of enablement. The Examiner states that a skilled person in the art would not have known what an influenza B or C protein "similar" to M2 is. Applicants have amended independent claims 26 and 54 (and claim 46, for that matter) to more particularly point that the "similar" influenza B and C proteins mean NB and CM2, respectively.

The Examiner further contends that applicants have not presented evidence demonstrating that M2 is truly conserved among influenza A isolates. Applicants point out that Table 1 of the specification (p. 4) provides such evidence. Table 1 lists extracellular domain sequences of fourteen influenza A isolates collected over a span of 56 years (1933 to 1989). Twelve of the fourteen sequences, including the 1933 isolates and the 1989 isolate, are identical – SEQ ID NO:1. The remaining two sequences differ from SEQ ID NO:1 in no more than 3 positions.

During the interview, applicants' representatives presented a table showing a total of 54 M2 extracellular sequences from isolates collected over a span of almost seven decades (Exhibit 1 attached hereto). Thirty nine (39) of the 54 sequences,

including the first (1933) and last ones (1999), are SEQ ID NO:1, with the remaining ones having variations in limited positions. This high degree of conservation is especially remarkable in view of the notoriously high mutation rates for the other two influenza membrane proteins – the N and H proteins.

In the Office Action, the Examiner maintains that Slepushkin's statement about "lower durability and/or activity" of M2 immunization remains relevant. During the interview, the Examiner stated that her underlying concern was that the mouse model disclosed in the specification might not be predictive of the vaccines' efficacy in humans. Thus, the Examiner invited applicants to submit evidence demonstrating the validity of this animal model in human influenza vaccine studies.

Applicants submit 48 such references, all of which were published no later than October 1997, the EP priority date of this application.[3] For the convenience of the Examiner, applicants also enclose a synopsis of the references (Exhibit 2). As shall be seen, each of these references describes influenza challenge experiments in mice. Nearly all involve testing and development of human flu vaccines.

Claim 32 stands rejected for lack of enablement. The Examiner contends that the specification does not teach how one could identify influenza-specific T helper or cytotoxic T cell epitopes. Office Action, p. 7. During the interview, the Examiner invited applicants to submit evidence demonstrating that methods for identification of such epitopes were well known in the prior art.

As pointed out in applicants' previous Response, T cell epitopes have been studied extensively in immunology, and there are standard methods to identify them (p.

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3 Copies of the references are forthcoming.

15). In that Response, applicants also pointed to four references that demonstrated this fact (p. 15). Applicants submit herewith 16 additional references.[4] These show that tens of T cell epitopes of various influenza A viral proteins have been identified (Exhibit 3). Collectively, all 20 references show that identification of T cell epitopes of influenza proteins is a routine matter. Thus, the Examiner's concern is overcome.

Certified Copy of Priority Document

Applicants submit herewith a certified copy of EP 97202434.3, the priority application of this application. 35 U.S.C. § 119(b).

CONCLUSION

Applicants respectfully submit that the claims, as amended, are in condition for allowance. Applicants request early, favorable action from the Examiner.

To expedite prosecution, the Examiner is invited to telephone applicants' undersigned representatives to discuss any issues that may remain.

Respectfully submitted,

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4 Copies of the references are forthcoming.